

### REMARKS

Claims 1, 5-33, and 38-42 are pending. Claims 1, 11, 15, 17, 29, 30, and 31 are currently amended. Claims 2-4, 10, 19-28, and 34-75 have been cancelled. Applicants request that Claims 14-18 and 29-33, previously withdrawn from consideration, be considered in light of claim amendments presented herein. Thus, Claims 1, 5-9, 11-18, and 29-33 are currently pending and presented for examination.

Support for the claim amendments are found throughout the specification and in particular, on page 11 at lines 11-12, page 13 at lines 1-2, page 13 at lines 12-15, page 14 at lines 3-5, and page 15 at lines 26-30. The amendments do not introduce new matter.

#### Request to Consider Claims to Nonelected Species

In the Office Action mailed December 2, 2004, it was noted that, upon allowance of a generic claim, applicant will be entitled to consideration of claims to additional species. With respect to Claims 29-33 to nonelected species, Applicants request consideration of these claims as provided by 37 C.F.R. §1.141(a) if generic claims are found allowable.

#### Withdrawn Rejections and Objections

Applicants thank the Examiner for withdrawing objections to the claims, and for withdrawing previous claim rejections under 35 U.S.C. §112, first paragraph, 35 U.S.C. §102(b), and 103(a).

#### Maintained Claim Rejections

Rejection of Claims 19-21 under 35 U.S.C. §112, first paragraph, has been maintained in the Office Action. Claims 19-21 have been cancelled, thereby rendering this rejection moot.

#### New Claim Rejections Following Amendment

##### Rejections under 35 U.S.C. §102

##### *Rejection of Claims 1, 5-13, and 22-24 under 35 U.S.C. §102(a)*

Claims 1, 5-13, and 22-24 stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by slides from a presentation to the Trustees of the Edinburgh Botanical Garden in June of 2003, submitted as IDS Reference DR on April 12, 2004, on grounds that the slides are allegedly "by another." Applicants disagree. The slides are not "by another" and furthermore, the slides do not teach the claimed invention.

The term "others" in 35 U.S.C. §102(a) refers to any entity which is different from the inventive entity. MPEP §2132.III On the second page of the printed version of the slides, the author, author's institutional affiliation, location, and date of the talk are set forth, clearly showing that the slides were authored by Paul Alan Cox.

Further, a reference must teach every element of the claim in order to anticipate the claim. MPEP §2131. The disclosure in the slides from the Edinburgh Botanical Garden presentation does not disclose a method of screening a human subject having or at risk of having a neurological disorder by analyzing a keratinous tissue sample from the subject to determine the presence of  $\beta$ -N-methylamino-L-alanine (BMAA) or a BMAA derivative, as claimed herein. For all the reasons presented above, the present rejection under 35 U.S.C. §102(a) is improper and should be withdrawn.

*Rejection of Claims 1, 7-10, 22, and 23 under 35 U.S.C. §102(b)*

Claims 1, 7-10, 22, and 23 stand rejected under 35 U.S.C. §102(b) over Perry *et al.* (1990, *Ann Neurol* 29:12-17), on grounds that Perry allegedly discloses methods of detecting BMAA in cerebrospinal fluid. Applicants disagree. Applicants note that Claims 10, 22, and 23 have been cancelled, thereby obviating the rejection with respect to these claims.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1052 (Fed. Cir. 1987), cited at MPEP §2131. Here, Claim 1 recites a method of screening a human subject having or at risk of having a neurological disorder by analyzing a keratinous tissue sample from the subject to determine the presence of BMAA or a BMAA derivative. Perry *et al.* does not disclose determining BMAA in a keratinous tissue sample. Because the cited reference does not teach each and every element of Claim 1 and claims dependent therefrom, the rejection under 35 U.S.C. §102(b) over Perry *et al.* is improper and should be withdrawn.

Rejections under 35 U.S.C. §103

*Rejection of Claims 1, 7-12, and 22-24 under 35 U.S.C. §103(a)*

Claims 1, 7-12, and 22-24 stand rejected under 35 U.S.C. §103(a) over Perry *et al.* (1990, *Ann Neurology* 29:12-17), Kisby *et al.* (1988, *J Neuroscience Meth* 26:45-54), Cox *et al.* (2002, *Neurology* 58:956-959), and Banack *et al.* (2002, ESA Annual Meeting, Oral Session #89). According to the Office Action, "[i]t would have been

obvious to one of ordinary skill in the art to test a human brain sample for the presence of BMAA,” where the motivation to test a human brain sample “would be to detect the presence of a neurotoxin, which is indicative of disease” and “it would be reasonable to expect success when performing the method on human brain tissue. (Office Action, page 6, lines 3-6) Applicants disagree. Applicants note that Claims 10 and 22-24 have been cancelled, thereby obviating this rejection with respect to those claims.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See*, MPEP §§ 2142, 2143. As shown below, no *prima facie* case of obviousness has been established for any rejected claim and therefore, the claim rejections under 35 U.S.C. §103(a) should be withdrawn.

*Cited references do not teach the claimed invention.*

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. MPEP §2143.03, citing *In re Royka*, 180 USPQ 580 (CCPA 1974). Here, Claim 1 recites a method of screening a human subject having or at risk of having a neurological disorder by analyzing a keratinous tissue sample from the subject to determine the presence of BMAA or a BMAA derivative. Neither Perry *et al.*, nor Kisby *et al.*, nor Cox *et al.* nor Banack *et al.*, alone or in combination, teaches or suggests a method of screening a human subject by analyzing a keratinous tissue sample from the subject to determine the presence of BMAA or a BMAA derivative. Because the cited combination of references does not teach or suggest all the claim limitations of Claim 1, no *prima facie* case of obviousness has been established.

*No motivation to combine or modify the references*

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. MPEP §2143.01. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. MPEP §2143, citing *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). Here, no teaching or

suggestion is found in the prior art to screen a human subject having or at risk of having a neurological disorder by analyzing a keratinous tissue sample from the subject to determine the presence of BMAA or a BMAA derivative. Without motivation to combine the teachings to make the claimed invention, no *prima facie* case of obviousness has been established.

Because no *prima facie* case of obviousness has been established, the rejection of Claims 1, 7-12, and 22-24 under 35 U.S.C. §103(a) should be withdrawn.

*Rejection of Claims 5 and 6 under 35 U.S.C. §103(a)*

Claims 5 and 6 stand rejected under 35 U.S.C. §103(a) over Perry *et al.*, Kisby *et al.*, Cox *et al.*, and Banack *et al.* as applied to Claim 1, and further in view of Duncan *et al.* (1990, *Neurology* 40:767) and Duncan *et al.* (1992, *J Neurosci* 12:1523-2537). Here, the cited references do not teach the claimed invention. Further, the cited combination of references was improper because the Duncan *et al.* references teach away from combining or modifying the references to make the claimed invention.

*Cited references do not teach the claimed invention*

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. MPEP §2143.03, citing *In re Royka*, 180 USPQ 580 (CCPA 1974). Claim 1 recites, *inter alia*, analyzing a keratinous tissue sample from the subject to determine the presence of BMAA or a BMAA derivative. Perry *et al.*, Kisby *et al.*, Cox *et al.*, or Banack *et al.* fail to teach or suggest determining the presence of BMAA or a BMAA derivative in a keratinous tissue sample from a human subject. The Duncan *et al.* references fail to cure this deficiency, as neither Duncan *et al.* reference discloses or suggests determining the presence of BMAA or a BMAA derivative in a keratinous tissue sample from a human subject. Because the references fail to teach or suggest the claimed invention, no *prima facie* case of obviousness has been established.

*Cited references teach away from combining or modifying the references*

Furthermore, the cited Duncan *et al.* references actually teach away from modifying the references to practice the claimed invention. A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. MPEP §2141.02, citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303 (Fed. Cir. 1983). It is improper to combine references where the references teach away from their combination. MPEP §2145.X.D.2, citing *In re Grasselli*, 218 USPQ 769, 779 (Fed. Cir. 1983). Applicants point out that the

subtitle of Duncan *et al.* (1990) states that BMAA is “[a]n unlikely cause of amyotrophic lateral sclerosis and parkinsonism-dementia in Guam.” Further, Duncan *et al.* (1992) notes that they “have argued that there is insufficient evidence to link BMAA causally to neurological disorders” (page 1523, right column, lines 11-12) and proposes zinc as the neurotoxin in cycad flour (*see, e.g.*, title on page 1523 and concluding paragraphs on page 1536). Given that the Duncan references appear to teach away from measuring BMAA in a tissue sample, the combination of references relied upon to reject Claims 5 and 6 under 35 U.S.C. §103(a) is improper.

Because no *prima facie* case of obviousness has been established and because the combination of references relied upon is improper, the rejection of Claims 5 and 6 under 35 U.S.C. §103(a) should be withdrawn.

*Rejection of Claim 13 under 35 U.S.C. §103(a)*

Claim 13 stands rejected under 35 U.S.C. §103(a) over Perry *et al.*, Kisby *et al.*, Cox *et al.*, and Banack *et al.*, as applied to Claim 11, further in view of Schmidt *et al.* (1988, *Acta Neuropathol* 95:117-122) and Forman *et al.* (2002, *Am J Pathol* 160:1725-1731). It is admitted that none of Perry *et al.*, Kisby *et al.*, Cox *et al.*, or Banack *et al.* teach detecting BMAA in patients with Alzheimer’s disease (OA, page 7, lines 1-2), and it is asserted that motivation to combine the references is based on disclosures in Schmidt *et al.* and Forman *et al.* (OA, page 7, lines 11-12). Applicants disagree.

*Cited references do not teach the claimed invention*

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. MPEP §2143.03, citing *In re Royka* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Claim 13, dependent on Claim 11, which is dependent on Claim 1, recites screening a human subject having or at risk of having a neurological disorder by analyzing a keratinous tissue sample from a human subject to determine the presence of BMAA or a BMAA derivative, wherein the neurological disorder is Alzheimer’s disease. It is admitted that Perry *et al.*, Kisby *et al.*, Cox *et al.*, or Banack *et al.* fail to disclose detecting BMAA in patients with Alzheimer’s disease. As noted above, Perry *et al.*, Kisby *et al.*, Cox *et al.*, and Banack *et al.* fail to disclose detecting BMAA in a keratinous tissue sample from a human subject. Schmidt *et al.* and Forman *et al.* do not cure this deficiency, as neither reference teaches or suggests detecting BMAA in patients with Alzheimer’s disease, let alone detecting BMAA in a keratinous tissue sample from a subject. Because the cited

references do not teach or suggest the claimed invention, no *prima facie* case of obviousness has been established.

*No motivation to combine or modify the cited references*

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. MPEP §2143.01. It is asserted the motivation [to combine the references] would be to diagnose Alzheimer's disease, based on Schmidt *et al.* and Forman *et al.*, who allegedly "teach that similar mechanisms underlie the pathologies of both diseases" (OA, page 7, lines 11-12). Applicants disagree. Here, neither reference provides motivation to modify Perry *et al.*, Kisby *et al.*, Cox *et al.*, and Banack *et al.* to practice the claimed invention.

In fact, both references teach differences as well as similarities between the ALS-PDC and Alzheimer's disease, such that the references cannot be relied upon as allegedly teaching similar mechanisms underlying the pathologies of the diseases. Schmidt *et al.* allegedly teaches that patients with ALS-PDC and Alzheimer's disease "have amyloid plaques that are similar" (OA page 7, lines 2-3), and yet "was unable to detect the tau abnormalities that are typical of Alzheimer's disease" (OA page 7, lines 3-4). In fact, Schmidt *et al.* contrasts and distinguishes ALS-PDC from Alzheimer's disease. Likewise, despite the assertion that Forman *et al.* teaches similarities in tau and alpha-synuclein deposits, and allegedly suggests a common disease mechanism for ALS-PDC and Alzheimer's (OA page 7 at lines 6-7), the text in Forman *et al.* relied upon in the Office Action actually contrasts the two diseases by also pointing out that despite the similarities, in the case of ALS-PDC, these proteins aggregate independent of  $\beta$ -amyloid (page 1730, final paragraph). Forman *et al.* points out other differences between the diseases, *e.g.*, on page 1725, right column, lines 13-17.

Because both references teach differences as well as similarities between ALS-PDC and Alzheimer's disease, these references cannot be relied upon to provide motivation to modify Perry *et al.*, Kisby *et al.*, Cox *et al.*, and Banack *et al.* to practice the claimed invention. Therefore, no *prima facie* case of obviousness has been established and the rejection of Claim 13 under 35 U.S.C. §103(a) should be withdrawn.

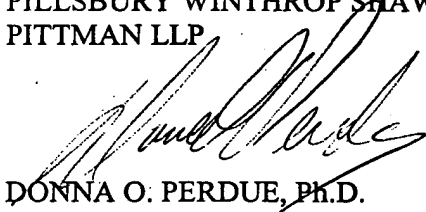
CONCLUSION

Claims 1, 5-33 and 38-42 are pending. Claims 1, 11, 15, 17, 29, 30, and 31 are currently amended. Claims 2-4, 10, 19-28, and 34-75 have been cancelled. Claims 1, 5-9, 11-18, and 29-33 are currently pending and presented for examination. Applicants request entry of the amendments presented herein. Applicants submit that, in light of the amendments and remarks presented herein, Claims 1, 5-9, 11-18, and 29-33 are now in condition for allowance.

Applicants believes that no fees are due. If any fees are due, please charge any fees associated with the submission of this paper to Deposit Account Number 03-3975. The Commissioner for Patents is also authorized to credit any over payments to the above-referenced Deposit Account.

Respectfully submitted,

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CERTIFICATION UNDER 37 C.F.R. §§ 1.8 and/or 1.10\*

I hereby certify that, on the date shown below, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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\* Only the date of filing (§ 1.6) will be the date used in a patent term adjustment calculation, although the date on any certificate of mailing or transmission under § 1.8 continues to be taken into account in determining timeliness. See § 1.703(f). Consider "Express Mail Post Office to Addressee" (§ 1.10) or facsimile transmission (§ 1.6(d)) for the reply to be accorded the earliest possible filing date for patent term adjustment calculations.